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VB

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/038,261	03/10/98	RIETER R	30435.54USU1

HM22/1206

MANDEL AND ADRIANO
35 N ARROYO PARKWAY, SUITE 60
PASADENA CA 91103

EXAMINER
HELMS,L

ART UNIT	PAPER NUMBER
1642	12

DATE MAILED: 12/06/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/038,261	Relter et al
Examiner	**Group Art Unit**
Larry R. Helms Ph.D.	1642

☒ Responsive to communication(s) filed on *17 Sep 1999*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *44-48* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *44-48* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

☒ NOTICE TO COMPLY WITH SEQUENCE REQUIREMENTS

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Applicant's election with traverse of Group IX, claim 43, in Paper No. 10 is acknowledged. The traversal is on the ground(s) that "the claims of Group 2 depend, directly or indirectly, upon the claims of Group 1. The claims in theses groups are dependent on each other because the nucleic acid molecules of Group 2 encode the proteins of Group 1. Further, the method of detection and killing claims (of Groups 4-9) involve the use of the antibodies or nucleic acid molecules of Groups 1-2". In addition applicants argue that "search of the art with regard to the invention of Groups 1-9 would not place an undue burden on the Examiner". This is not persuasive because Paper # 6 properly sets forth reasons for the distinction between groups I and II and groups I-IX. Applicant has provided no evidence to establish why the requirement for restriction is improper. As to the question of burden of search, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Further, it is doubted that applicant would readily accept the rejection of the process of the elected invention over a reference which relates only to the starting material. Clearly different searches and issues are involved in the examination of each group as set forth in paper # 6. Moreover, the applicants traversal of the restriction requirement is moot for the

applicants have canceled claims 1-43 without prejudice in paper # 10. For these reasons the restriction requirement is deemed to be proper and is made **FINAL**.

Claims 44-48 have been added and are examined on the merits.

Specification

2. The following are objected to in the Specification:

a. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed, for example, Monoclonal antibodies and methods for PSCA.

b. The first line in the Specification should clearly indicate whether application 08/814,279 is a CIP, divisional, or continuation. The relationship of 08/814,279 needs to be stated in line 5.

c. The Brief Description of the Drawings, pages 4-6, is incomplete as it lacks a separate description for Figures and it lacks SEQ ID NOs. The Brief Description of the Drawings need to be amended so that Figures recite separate descriptions for each view that match the labels for the Drawings. Also any reference to the figures in the specification needs to be amended accordingly.

d. The Abstract is objected to for it does not refer to the claimed antibodies or methods.

e. The amendments on page 5, lines 21, 24, and 30 of the specification, filed 9/17/99, has not been entered because the text was not found at that position.

Drawings

3. The drawings are considered to be informal because they fail to comply with 37 CFR 1.84(a)(1) which requires black and white drawings using India ink or its equivalent.

a. Photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) or (b)(1) is granted permitting their use as formal drawings. In the event applicant wishes to use the drawings currently on file as formal drawings, a petition must be filed for acceptance of the photographs or color drawings as formal drawings. Any such petition must be accompanied by the appropriate fee as set forth in 37 CFR 1.17(I), three sets of drawings or photographs, as appropriate, and, if filed under the provisions of 37 CFR 1.84(a)(2), an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The file of this patent contains at least one drawing executed in color. Copies of this patent with color drawing(s) will be provided by the Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

b. Figures 4 and 5 are illegible for examination purposes.

c. Figures need to be labeled separately, for example, Figure 1A, Figure 1B, Figure 7A, Figure 7B, Figure 9A, Figure 9B, Figure 11A, Figure 11B, Figure 11C, Figure 12A, Figure 12B, and Figure 12C.

Sequence requirements

4. This application contains sequence disclosures on page 12 line 29, for example, and in the Figures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821-1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

It is noted that SEQ ID NO:1 and SEQ ID NO:2 in a related application 09/251,835 was used in the instant application to search the antigen bound by the claimed antibody. The comparison of the sequences designated as SEQ ID NOS:1 and 2, (in Figures 1A and 1B) which is the sequence for the nucleic acid and the amino acid sequence, respectfully, for human PSCA in the related application 09/251,835, resulted in the conclusion that these sequences appear to be identical to those in Figures 1A and 1B of the instant application.

Any questions regarding compliance with the sequence rules requirements specifically should be directed to the departments listed at the bottom of the Notice to Comply.

APPLICANT IS GIVEN THE TIME ALLOTTED IN THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 C.R.F. §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 C.F.R. § 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 C.F.R. § 1.136. In no case may an applicant extend the period for response beyond the six month statutory period. Direct the response to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the response or canceling the sequences in the specification will obviate this objection.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 44-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 44 and 48 are indefinite as being structured as an improper Markush claims. (See MPEP 2173.05(h)). Proper Markush claims are in the format of "X is selected from a group consisting of A, B, C, and D," or "the X is A, B, C or D". It appears that perhaps the phrase "an antibody from the group consisting of" is unnecessary. Deletion of this phrase would be sufficient to obviate this indefiniteness.

b. Claims 44-48 are indefinite because they contain the abbreviation "PSCA" in claims 44 and 48. Full terminology should be in first instance of the claims followed by the abbreviation in parentheses. Dependent claims may then use the abbreviation. Abbreviations render the claim indefinite because the same abbreviation may represent more than one element or concept.

c. Claims 44-48 are indefinite for reciting in base claim 44 and 48 the laboratory designations "1G8, 2H5, 3C5, 3E6, and 4A10" because other laboratories/inventors may use the same laboratory designation to refer to different hybridomas. Amendment of the claim to insert the corresponding ATCC accession number of the hybridoma which produces the antibody or to add the SEQ ID Nos of the heavy and light chain variable regions would overcome this rejection. As written, it is impossible for one skilled in the art to determine the metes and bounds of the claims.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 44-48 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

a. Claims 44-48 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

b. It is unclear if a cell lines which produces an antibodies having the exact chemical identity of 1G8, 3C5, 2H5, 3E6, or 4A10 are known and publicly available, or can be reproducibly isolated without undue experimentation. Therefore, a suitable deposit for patent purposes is suggested. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of: (1) the claimed cell line; (2) a cell line which produces the chemically and functionally distinct antibody claimed; and/or (3) the claimed antibody's amino acid or nucleic acid sequence is an unpredictable event.

c. For example, very different V_H chains (about 50% homologous) can combine with the same V_K chain to produce antibody-binding sites with nearly the same size, shape, antigen specificity, and affinity. A similar phenomenon can also occur when different V_H sequences combine with different V_K sequences to produce antibodies with very similar properties. The results indicate that divergent variable region sequences, both in and out of the complementarity-determining regions, can be folded to form similar binding site contours, which result in similar immunochemical characteristics. [FUNDAMENTAL IMMUNOLOGY 242 (William E. Paul, M.D. ed., 3d ed. 1993)]. Therefore, it would require undue experimentation to reproduce the claimed antibody species 1G8, 3C5, 2H5, 3E6, or 4A10. Deposit of the hybridoma would satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See, 37 C.F.R. 1.801-1.809.

d. Applicants referral to the deposit of 1G8, 3C5, 2H5, 3E6, or 4A10 with ATCC # in the claims is an insufficient assurance that the required deposit has been made and all the conditions of 37 CFR 1.801-1.809 met. The specification is lacking the date of the deposit and the full address of the ATCC as well as assurance that the hybridomas will become available should the patent issue.

9. Claims 44-47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

a. Factors to be considered in determining whether undue experimentation is required, are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

b. The claims are broadly drawn to a method of inhibiting the growth of tumor cells expressing PSCA, comprising administering to a patient an antibody which binds specifically to the extracellular domain of PSCA in an amount to inhibit growth of the tumor. Further, the claims broadly encompass wherein the antibody is conjugated to a cytotoxic agent or a radioisotope. The claims broadly encompass administering the antibody to any patient including humans as well as administering the antibody that is not conjugated to a toxic agent.

c. The specification teaches the expression of PSCA in murine samples of spleen, liver, prostate, kidney, and testis (page 30, lines 29-31) and in LPAC-4 xenograft tumors as well as the expression in paraffin-embedded prostate cancer specimens by mRNA in situ hybridization (page 31, lines 23-25). The specification teaches FACS analysis was used to localize PSCA expression to the cell surface utilizing antibodies and 293T and LAPC-4 cells (page 33, lines 28-30 and

figure 12C). The specification fails to enable the use of the unconjugated antibodies for inhibition of growth of prostate tumor cells in vivo as well as conjugates to the antibody. The specification lacks guidance as to the methods of administering the antibody, the amounts for administering, the timing for administering, and as the patient to whom the antibody is to be administered to.

d. The use of antibody immunotherapy for the in vivo treatment of tumors has been shown to have limitations. Jain discloses the art known barriers to the delivery of drugs into solid tumors (Scientific American July 1994). Impediments to drug delivery include (1) Nonuniform blood delivery to all areas of the tumor in which some areas of the tumor receive therapeutic agents and other areas of the tumor receive no therapeutic agent at all. (Page 60 col. 3); (2) Increased viscosity of blood in the tumor itself which also hinders drug delivery to the tumor (see paragraph bridging pages 60 and 61); (3) High liquid pressures in the interstitial matrix can retard the delivery of large therapeutic agents, such as antibodies, into tumors (page 61, Col. 1 paragraph 1); (4) Convection is a necessary mechanism by which larger therapeutics molecules such as antibodies, reach target cells which are not directly fed by the vasculature. Convection is not observed in large tumors (defined as more than ½ centimeter in diameter, page 62 col. 1) and convection is necessary for adequate drug delivery of molecules having a molecular weight of more than 5000 (page 61, col. 1 through page 63, col. 3) and (4) Molecules as large as antibodies (i.e., MW=150,000) would require several months to reach a uniform

concentration in a tumor that measures 1 centimeter in radius (page 63, col. 2). Prostate cancer can result in a solid tumor as evidenced by metastasis into various tissues such as bone.

e. Chatterjee et al state the art recognized experience that for any novel therapy, the transition for the laboratory to the clinic (animal experiments to the bedside) is a quantum leap (Cancer Immunol. Imunother., 1994, see Introduction). Chatterjee et al state results obtained under controlled conditions and in inbred animals often differ from the clinical response obtained in patients. Chatterjee et al state tumor burden and antigenic drift continue to present serious burdens for successful cancer therapy in vivo. In addition, Chatterjee et al state tumors are classified as immunogenic or non-immunogenic, solid or hematological in nature and effective cancer strategies should be designed to deal effectively with the nature of each of these classifications.

f. The specification does not disclose whether the method is effective in animals with pre-existing tumor, and this is a significant omission in view of the well-known immunosuppressive effects of certain tumors. The criticality of a working example encompassing all of the method steps, especially the treatment of pre-existing neoplasia, is underscored by Gura et al (Science Vol 278 11/97 1041-1042) in a discussion of potential shortcomings of extrapolating from in vitro studies and animal studies to similar procedures in cancer patients. Gura et al teaches that "xenograft tumors don't behave like naturally occurring tumors in humans" (page 1041, second col, second full paragraph) and that there were "gross difference in sensitivity in real tumors in mice and in the clonogenic assay" (page 1042, second

col, second full paragraph). Further, Gura teaches that in vitro clonogenic assays "cannot tell researchers how anticancer drugs will act in the body" (page 1042, first-second col, bridging paragraph). One skilled in the art would reasonably conclude that, even if it were disclosed in the specification, evidence obtained in mouse xenograft models would not necessarily correlate with results expected in humans patients.

g. As evidenced by Seaver (1994; Genetic Engineering Vol 14(14):pages 10 and 21), selection of an antibody as an immunotherapeutic agent is an unpredictable task as the antibody must possess sufficient specificity and a high degree of affinity for its target for use as an immunotherapeutic agent and because these qualities are dependent on the physiology of the particular pathology and the accessibility of the target antigen. The specification is silent concerning what sort of specificity and affinity would be necessary for the antibodies of the claimed immunotoxin so that one skilled in the art would not be able to practice the claimed invention without undue experimentation.

h. Further, the disclosure does not provide working examples wherein all of the steps required to practice the method are employed. Lack of working examples is given added weight in cases involving an unpredictable and undeveloped art such as the treatment in vivo of prostate cancer. In the instant case, the claims are so broadly drawn, the guidance is so limited, and the art is so unpredictable that skilled artisan is presented with a multitude of un-linked alternatives with no guidance as to which will enable use of the invention as claimed. Among these are (I) which antibody to use, (ii) which amount of the antibody is effective to inhibit growth, (iii) what

specificity and affinity is necessary, (iv) how to use the antibody alone (claim 44) which is not conjugated to a cytotoxic agent, (v) how in vitro results are expected to correlate with in vivo results in human patients, and (vi) what schedule, and route of administration will provide a successful therapeutic outcome.

I. Taken in view of the unpredictability of the art, as evidenced by Jian, Chatterjiee et al, Gura et al, and Seaver, the inadequate guidance and working examples in the specification, undue experimentation would be required to inhibit the growth of prostate tumors in vivo commensurate with the scope of the broadly written claims. Therefore, in weighing the factors to be considered in determining whether or not the practice of a claimed invention would require "undue" experimentation, as set forth In *In re Wands* (8 USPQ 2d at 1404), the weight of the analysis clearly favors a finding of "undue" experimentation.

Priority

10. The claims recite a method of inhibiting the growth of tumor cells expressing PSCA, comprising administering to a patient an antibody from the group consisting of 1G8, 3C5, 2H5, 3E6, or 4A10 which binds specifically to the extracellular domain of PSCA In an amount to inhibit growth of the tumor.

No evidence for written description of the claimed limitations of the monoclonal antibodies "1G8, 3C5, 2H5, 3E6, or 4A10" is seen in applications 08/814,279 or 60/071,141 for

which the instant application claims priority under 35 U.S.C. 120. Unfortunately application 60/074,675 was unavailable for inspection. The examiner is continuing to search for 60/074,675 and apologizes for any inadvertent inconvenience. Therefore, claims 44-48 are granted the priority date of the filing date of application 09/038,261, which is 3/10/98.

11. Claims 44-48 are free of the art. The nearest art that reads on the claims is Billing-Medel et al (WO 98/51805, 11/19/1998). Billing-Medel et al teach the PS116 protein (SEQ ID NO: 25) as well as antibodies to the protein (page 45-52), *In vivo* use, by administering to a patient suspected of having diseases of the prostate, of antibodies and conjugates (page 52, lines 32-35). The PS116 protein of Billing-Medel et al is identical to the PSCA protein in the instant application. Please see the attached sequence alignment to this Office Action. "Qy" is SEQ ID NO:2 of the instant application and "Db" is the database query of SEQ ID NO:25 of Billing-Medel et al. The Billing-Medel et al patent was published in 11/19/98. As set forth above the priority date granted to the instant application is 3/10/98, therefore the reference of Billing-Medel et al is not prior art on the instant claims.

It is noted that the art of Au-Young (US 5,856,136 filed July 3, 1996) teach antibodies and hybridomas to the SCAH-2 protein encoded by SEQ ID NO:2 (see column 2, lines 14-16 and 44-50, column 14, lines 22-32). The SCAH-2 protein of AU-Young is the identical antigen as PSCA in the instant invention (see SEQ ID NO:2 in Au-Young patent as compared to SEQ ID NO:2 from the related application 09/251,835). A sequence alignment for SEQ ID NO:2 of Au-

Young and SEQ ID NO:2 of the related application is attached to the back of this Office Action. "Qy" is the instant application SEQ ID NO:2 and "Db" is Au-Young SEQ ID NO:2. Au-Young, however, does not fairly teach or suggest the presence of the PSCA protein (SCAH-2) in prostate cells, or methods of inhibiting growth using antibodies specific to PSCA.

Summary

12. No Claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located In Crystal Mall 1. The faxing of such papers must conform with the notice published In the Official

Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Respectfully,

Larry R. Helms Ph.D.

JULIE BURKE
PRIMARY EXAMINER

ALIGNMENTS

RESULT 1
ID W86024 standard; Protein; 123 AA.
AC W86024;
DT 23-FEB-1999 (first entry)
DE UT116 polypeptide consensus sequence.
KW UT116; urinary tract; epitope; antigen; detection; diagnosing;
KW monitoring; in vivo imaging; cancer; agonist; antibody; tumour;
KW metastasis.
OS Homo sapiens.
PN WO9851824-A1.
PD 19-NOV-1998.
PF 15-MAY-1998; U09972.
PR 15-MAY-1997; US-856652.
PA (ABBO) ABBOTT LAB.
PI Billing-medel PA, Cohen M, Colpitts TL, Friedman PN,
PI Granados EN, Hodges SC, Klass MR, Kratochvil JD,
PI Roberts-rapp L, Russell JC, Stroupe SD;
DR WPI; 99-045237/04.
DR N-PSDB; V80396, V80397.
PT New method for detecting diseases of the urinary tract - comprises
PT use of a UT116 polynucleotide, protein or antibodies, used for
PT preventing and treating urinary tract infections and cancer
PS Claim 10; Page 94; 113pp; English.
CC This represents the consensus sequence of the UT116 polypeptide, derived
CC from urinary tract tissue. The invention relates to a method of detecting
CC the presence of a target UT116 polynucleotide in a test sample using
CC UT116 gene-specific sequences (V80386 to V80397). Host cells transfected
CC with an expression vector containing the UT116 gene can be used to
CC produce a UT116 polypeptide recombinantly. This polypeptide has at least
CC one UT116 epitope which can be used in a method for detecting UT116
CC antigen in a test sample. The polynucleotides and polypeptides are useful
CC for detecting, diagnosing, monitoring, staging, prognosticating, in vivo
CC imaging, preventing, treating or determining the predisposition of a
CC subject to diseases and conditions of the urinary tract, such as urinary
CC tract cancer. Antibodies specifically binding to an epitope of UT116
CC antigen, and agonists are useful for treating urinary tract diseases,
CC tumours and metastases.
SQ Sequence 123 AA;

Query Match 100.0%; Score 902; DB 38; Length 123;

Best Local Similarity 100.0%; Pred. No. 4.04e-78;
Matches 123; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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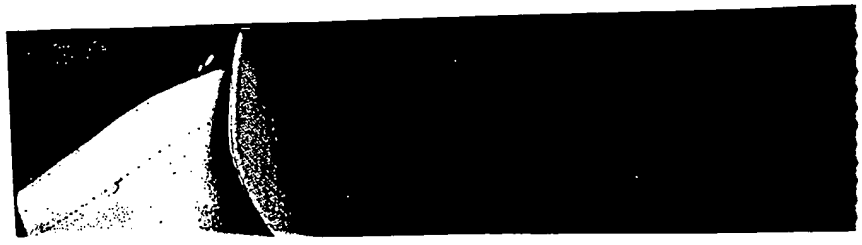
Db      1 mkavllallmaglalqpgtallcysckaqvsnedclqvenctqlgeqcwtariravgllt 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy      1 MKAVLLALLMAGLALQPGTALLCYSCKAQVSNEDCLQVENCTQLGEQCWTARIRAVGLLT 60

Db     61 viskgcslncvddsqdyyvgkknitccdtdlcnasgahalqpaaailallpalglllwgp 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy     61 VISKGCSLNCVDDSQDYYVGKKNITCCDTDLCNASGAHALQPAAAILALLPALGLLLWGP 120

Db    121 gql 123
          |||
Qy    121 GQL 123
```

XX
DE Sequence 2, Application US/08675508
XX
CC Sequence 2, Application US/08675508
CC Patent No. 5856136
CC GENERAL INFORMATION:
CC APPLICANT: Au-Young, Janice
CC TITLE OF INVENTION: NOVEL HUMAN STEM CELL ANTIGENS
CC NUMBER OF SEQUENCES: 26
CC CORRESPONDENCE ADDRESS:
CC ADDRESSEE: Incyte Pharmaceuticals, Inc.
CC STREET: 3174 Porter Drive
CC CITY: Palo Alto
CC STATE: CA
CC COUNTRY: U.S.
CC ZIP: 94304
CC COMPUTER READABLE FORM:
CC MEDIUM TYPE: Diskette
CC COMPUTER: IBM Compatible
CC OPERATING SYSTEM: DOS
CC SOFTWARE: FastSEQ Version 1.5
CC CURRENT APPLICATION DATA:
CC APPLICATION NUMBER: US/08/675,508
CC FILING DATE: Filed Herewith
CC ATTORNEY/AGENT INFORMATION:
CC NAME: Billings, Lucy J.
CC REGISTRATION NUMBER: 36,749
CC REFERENCE/DOCKET NUMBER: PF-0066 US
CC TELECOMMUNICATION INFORMATION:
CC TELEPHONE: 415-855-0555
CC TELEFAX: 415-845-4166
CC INFORMATION FOR SEQ ID NO: 2:
CC SEQUENCE CHARACTERISTICS:
CC LENGTH: 123 amino acids
CC TYPE: amino acid
CC STRANDEDNESS: single
CC TOPOLOGY: linear
CC MOLECULE TYPE: peptide
CC IMMEDIATE SOURCE:
CC LIBRARY: SCAH-2
CC CLONE:



SQ SEQUENCE 123 AA; 12951 MW; 71550 CN;

Query Match 99.6%; Score 898; DB 2; Length 123;
Best Local Similarity 99.2%; Pred. No. 6.44e-77;
Matches 122; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

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Db       1 MKAVLLALLMAGLALQPGTALLCYSCKAQVSNEDCLQVENCTQLGEQCWTARIRAVGLLT 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy       1 MKAVLLALLMAGLALQPGTALLCYSCKAQVSNEDCLQVENCTQLGEQCWTARIRAVGLLT 60

Db      61 VISKGCSLNCVDDSQDYYVGKKNITCCDTDLCNXSGAHALQPAAAILALLPALGLLLWGP 120
           |||||||||||||||||||||||||||||||| ||||||||||||||||||||||||||||
Qy      61 VISKGCSLNCVDDSQDYYVGKKNITCCDTDLCNASGAHALQPAAAILALLPALGLLLWGP 120

Db     121 GQL 123
           |||
Qy     121 GQL 123
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Application No.: 09/038261

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable form of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other: _____

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
For CRF Submission Help, call (703) 308-4212
For PatentIn software help, call (703) 308-6856

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